IMPORTANT SAFETY INFORMATION | FULL PRESCRIBING INFORMATION FOR CAPSULES

Pfizer Oncology is pleased to announce that IBRANCE® (palbociclib) is transitioning from capsules to tablets. The new film-coated tablets may be taken with or without food and will be dispensed in blister packs (rather than bottles). The blister packs are designed to enable patients to track where they are in their treatment cycle. The tablet formulation is bioequivalent to the capsule formulation. There is no change to the active ingredient, available dosage strengths or dosing schedule.

IBRANCE is indicated for the treatment of adult patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer in combination with:

- an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women or in men, or
- fulvestrant in patients with disease progression following endocrine therapy

A trade sheet for the tablet formulation (including the IBRANCE tablet full Prescribing Information) is attached for your reference.

<u>Frequently Asked Questions About the Transition From Capsules to Tablets</u>:

Why is IBRANCE transitioning from capsules to tablets?

As part of Pfizer's ongoing commitment to patients, Pfizer routinely looks for opportunities to better address patient needs and preferences. The IBRANCE tablet formulation offers patients:

- Increased flexibility: Patients can take IBRANCE tablets with or without food, and they can be coadministered with proton pump inhibitors (PPIs) or antacids
- Dose tracking: Tablets come in weekly blister packs that are designed to help patients track their treatment cycles
- Addresses dietary restrictions: The tablet formulation does not contain lactose (dairy) or gelatin

When is the transition happening?

Pfizer will transition to distributing the tablet formulation in April, 2020. At this point, prescriptions will need to specify whether the patient should receive capsules or tablets. Pfizer will continue to supply the capsule formulation for a limited period to enable practices to transition IBRANCE prescriptions to the new tablet formulation. NDC codes for the new formulation are included in the attached trade sheet.

When should I begin to stock IBRANCE tablets?

Please ensure you have some supply of IBRANCE tablets at the time of launch. Keep in mind that because prescriptions will need to specify capsules or tablets, a new prescription will be required if the formulation in stock differs from what is specified in the prescription.

What should I do with my existing inventory of IBRANCE capsules?

Where possible, use up remaining capsule inventory for existing patients that have yet to receive a prescription for the new tablet formulation.

Is there a difference in the active ingredient of IBRANCE?

The tablet formulation is bioequivalent to the capsule formulation. There is no change to the active ingredient, available dosage strengths or dosing schedule.

What should my patients know about the tablet formulation changes?

- IBRANCE tablets can be taken with or without food, are film-coated, and may be administered with proton pump inhibitors (PPIs) or antacids
- Patients should be advised not to crush, chew, or split the tablets before swallowing them
- The new tablets are provided in blister packs. The tablets must be stored in the original blister packs. Pill caddies should no longer be used
- The new tablets do not contain lactose or gelatin
- At launch, the cost for the tablet formulation will be the same as the capsules. We do not expect the new tablet formulation to have any impact on the cost of IBRANCE to patients, access or coverage

Will vouchers still be valid?

Vouchers in the market will be honored and are subject to the same terms and conditions.

Are there any changes to the way I bill for IBRANCE?

You will need to bill using the new NDCs for IBRANCE tablets.
New NDCs for IBRANCE include:

- NDC 0069-0688-03 – 125 mg
- NDC 0069-0486-03 – 100 mg
- NDC 0069-0284-03 – 75 mg
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How will the new form of IBRANCE be packaged?

IBRANCE tablets will be packaged in monthly boxes containing three blister packs of seven tablets each (21 tablets total). The new packaging may require additional shelf space as compared to bottles (see attached trade sheet for dimensions).

Important Safety Information

Neutropenia was the most frequently reported adverse reaction in PALOMA-2 (80%) and PALOMA-3 (83%). In PALOMA-2, Grade 3 (56%) or 4 (10%) decreased neutrophil counts were reported in patients receiving IBRANCE plus letrozole. In PALOMA-3, Grade 3 (55%) or Grade 4 (11%) decreased neutrophil counts were reported in patients receiving IBRANCE plus fulvestrant. Febrile neutropenia has been reported in 1.8% of patients exposed to IBRANCE across PALOMA-2 and PALOMA-3. One death due to neutropenic sepsis was observed in PALOMA-3. Inform patients to promptly report any fever.

Monitor complete blood count prior to starting IBRANCE, at the beginning of each cycle, on Day 15 of first 2 cycles and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

Severe, life-threatening, or fatal interstitial lung disease (ILD) and/or pneumonitis can occur in patients treated with CDK4/6 inhibitors, including IBRANCE when taken in combination with endocrine therapy. Across clinical trials (PALOMA-1, PALOMA-2, PALOMA-3), 1.0% of IBRANCE-treated patients had ILD/pneumonitis of any grade, 0.1% had Grade 3 or 4, and no fatal cases were reported. Additional cases of ILD/pneumonitis have been observed in the post-marketing setting, with fatalities reported.

Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis (e.g. hypoxia, cough, dyspnea). In patients who have new or worsening respiratory symptoms and are suspected to have developed pneumonitis, interrupt IBRANCE immediately and evaluate the patient. Permanently discontinue IBRANCE in patients with severe ILD or pneumonitis.

Based on the mechanism of action, IBRANCE can cause fetal harm. Advise females of reproductive potential to use effective contraception during IBRANCE treatment and for at least 3 weeks after the last dose. IBRANCE may impair fertility in males and has the potential to cause genotoxicity. Advise male patients to consider sperm preservation before taking IBRANCE. Advise male patients with female partners of reproductive potential to use effective contraception during IBRANCE treatment and for 3 months after the last dose. Advise females to inform their healthcare provider of a known or suspected pregnancy. Advise women not to breastfeed during IBRANCE treatment and for 3 weeks after the last dose because of the potential for serious adverse reactions in nursing infants.

The most common adverse reactions (≥10%) of any grade reported in PALOMA-2 for IBRANCE plus letrozole vs placebo plus letrozole were neutropenia (80% vs 6%), infections (60% vs 42%), leukopenia (39% vs 2%), fatigue (37% vs 28%), nausea (35% vs 26%), alopecia (33% vs 16%), stomatitis (30% vs 14%), diarrhea (26% vs 19%), anemia (24% vs 9%), rash (18% vs 12%), asthenia (17% vs 12%), thrombocytopenia (16% vs 1%), vomiting (16% vs 17%), decreased appetite (15% vs 9%), dry skin (12% vs 6%), pyrexia (12% vs 9%), and dysgeusia (10% vs 5%).

The most frequently reported Grade ≥3 adverse reactions (≥5%) in PALOMA-2 for IBRANCE plus letrozole vs placebo plus letrozole were neutropenia (66% vs 2%), leukopenia (25% vs 0%), infections (7% vs 3%), and anemia (5% vs 2%).

Lab abnormalities of any grade occurring in PALOMA-2 for IBRANCE plus letrozole vs placebo plus letrozole were decreased WBC (97% vs 25%), decreased neutrophils (95% vs 20%), anemia (78% vs 42%), decreased platelets (63% vs 14%), increased aspartate aminotransferase (52% vs 34%), and increased alanine aminotransferase (43% vs 30%).

The most common adverse reactions (≥10%) of any grade reported in PALOMA-3 for IBRANCE plus fulvestrant vs placebo plus fulvestrant were neutropenia (83% vs 4%), leukopenia (53% vs 5%), infections (47% vs 31%), fatigue (41% vs 29%), nausea (34% vs 28%), anemia (30% vs 13%), stomatitis (28% vs 13%), diarrhea (24% vs 19%), thrombocytopenia (23% vs 0%), vomiting (19% vs 15%), alopecia (18% vs 6%), rash (17% vs 6%), decreased appetite (16% vs 8%), and pyrexia (13% vs 5%).

The most frequently reported Grade ≥3 adverse reactions (≥5%) in PALOMA-3 for IBRANCE plus fulvestrant vs placebo plus fulvestrant were neutropenia (66% vs 1%) and leukopenia (31% vs 2%).
Lab abnormalities of any grade occurring in PALOMA-3 for IBRANCE plus fulvestrant vs placebo plus fulvestrant were decreased WBC (99% vs 26%), decreased neutrophils (96% vs 14%), anemia (78% vs 40%), decreased platelets (62% vs 10%), increased aspartate aminotransferase (43% vs 48%), and increased alanine aminotransferase (36% vs 34%).

Avoid concurrent use of strong CYP3A inhibitors. If patients must be administered a strong CYP3A inhibitor, reduce the IBRANCE dose to 75 mg. If the strong inhibitor is discontinued, increase the IBRANCE dose (after 3-5 half-lives of the inhibitor) to the dose used prior to the initiation of the strong CYP3A inhibitor. Grapefruit or grapefruit juice may increase plasma concentrations of IBRANCE and should be avoided. Avoid concomitant use of strong CYP3A inducers. The dose of sensitive CYP3A substrates with a narrow therapeutic index may need to be reduced as IBRANCE may increase their exposure.

For patients with severe hepatic impairment (Child-Pugh class C), the recommended dose of IBRANCE is 75 mg. The pharmacokinetics of IBRANCE have not been studied in patients requiring hemodialysis.